Review

Passive Smoking and the Risk of Heart Disease

Kyle Steenland, PhD

Objective.—This paper reviews the evidence that exposure to environmental tobacco smoke (ETS) increases the risk of heart disease death among persons who have never smoked (never-smokers). The annual number of heart disease deaths in the United States attributable to ETS is estimated, as is the individual risk of heart disease death for exposed never-smokers.

Data Sources.—Nine epidemiologic studies and numerous experimental studies are available to evaluate the association of ETS and heart disease.

Data Synthesis.—The relative risk for never-smokers living with current or former smokers, compared with never-smokers living with nonsmokers, has ranged from 0.9 to 3.0 in nine studies. Seven studies were positive, one was positive for women but not men, and one was negative. Several studies have shown a dose-response relationship and have controlled for other risk factors. Evidence from experimental studies suggests that ETS can damage the cardiovascular system, via both short-term and long-term mechanisms. Assuming that the observed heart disease risk for those exposed to ETS is not an artifact of misclassification or confounding, approximately 35 000 to 40 000 deaths from ischemic heart disease among never-smokers and long-term former smokers are estimated to have occurred annually in the United States as a result of ETS exposure in the early 1980s. An individual male never-smoker living with a current or former smoker is estimated to have an approximately 9.6% chance of dying of ischemic heart disease by the age of 74 years, compared with a 7.4% chance for a male never-smoker living with a nonsmoker. The corresponding lifetime risks for women are 6.1% and 4.9%.

Conclusions.—The public health burden due to ETS exposure is likely to be much greater for heart disease than for lung cancer, which has been the focus of most debate to date. Individual lifetime excess risks of heart disease death due to ETS of one to three per 100 can be compared with much lower excess risks of one death per 100 000, which are often used in determining environmental limits for other toxins. Exposure to ETS is not currently regulated at the federal level, except for domestic air traffic.

(*JAMA*. 1992;267:94-99)

ENVIRONMENTAL tobacco smoke (ETS) has been associated with a variety of diseases, particularly lung cancer. In 1986, the National Research Council[1] estimated that about 3000 lung cancer cases per year among persons in the United States who had never smoked (never-smokers) were attributable to ETS. In 1990, the Environmental Protection Agency published a draft report reaching similar conclusions.[2] While the lung cancer risk among never-smokers exposed to ETS is well established, a possible risk of heart disease due to ETS is more controversial. Yet the epidemiologic evidence for a heart disease effect has been increasing in the last several years. This article discusses the available data on ETS and heart disease. Based on the assumption that the epidemiologic studies are reasonably accurate, the annual number of deaths in the United States due to ischemic heart disease (IHD) attributable to ETS is estimated, as well as the individual lifetime risk of IHD death due to ETS.

From the National Institute for Occupational Safety and Health, Cincinnati, Ohio

Reprint requests to the National Institute for Occupational Safety and Health, Mailstop R13, 4676 Columbia Pkwy, Cincinnati, OH 45226 (Dr Steenland)

DATA ON ETS EXPOSURE

Environmental tobacco smoke is difficult to measure directly. Indirect measures that have been used are airborne respirable suspended particulate (defined as particles of less than 2.5-μm diameter) and urinary cotinine (a metabolite of nicotine). Passive monitors of vapor-phase nicotine are a promising new direct method to measure ETS.[3]

Repace[4] has shown that the background level of respirable suspended particulate (approximately 20 μg/m³) doubles in homes in which a smoker lives. ETS exposure also occurs outside the home. Approximately 28% of the US adult population smokes, and ETS exposure occurs in most indoor environments. Cummings et al[5] have shown that 91% of 663 nonsmokers had cotinine in their urine, including 81% of the 162 subjects who reported no exposure to ETS in the previous 4 days (the relevant period for cotinine measurement). The average level of cotinine in the urine of nonsmokers was about 8 ng/mL, compared with about 1200 ng/mL in smokers. Other investigators[6,7] have shown that nonsmokers living with smokers have 2.5 to 3 times the level of urinary cotinine compared with that of nonsmokers living with nonsmokers.

The relative contribution of ETS exposure at work to total exposure is not well known. Nonsmoking restaurant workers (perhaps a worst case for occupational ETS exposure) averaged 56 ng/mL of urinary cotinine in one study.[6] Conversely, Haley et al[8] have shown in a limited sample that urinary cotinine for those exposed at home and at work increased only slightly compared with those exposed only at home.

The National Research Council[1] concluded that nonsmokers exposed to passive smoke are absorbing the equivalent of 0.1 to 1.0 cigarettes a day, based on urinary cotinine levels. However, the constituents of sidestream smoke are different from those of inhaled mainstream smoke. Sidestream smoke is generated at a lower temperature than mainstream smoke, the particle size is smaller, less of the generated smoke is particulate, and the pH is higher.[1] There are more carbon monoxide and nicotine breakdown products in dilute sidestream smoke than in mainstream smoke. These differences imply that it is difficult to determine the relative toxicity of sidestream smoke vs mainstream smoke. Consequently, arguments inferring ETS

Table 1.—Heart Disease Among Never-Smokers Due to ETS*

Source	Type and Size	Exposure	Rate Ratio (95% CI) (No. of Observed Deaths)	Comment
Hole et al[11]	12-y follow-up, 3960 men, 4037 women	Living with smoker or ex-smoker in early 1970s (self-report)	2.01 (1.21-3.35) (455)	Adjusted for 3 CV risk factors and social class, dose response
Humble et al[12]	20-y follow-up, 513 women aged 40+ y	Living with smoker in 1960 (self-report)	1.59 (0.99-2.57) (76)	Adjusted for 3 CV risk factors, dose response in some strata
Hasleing et al[13]	12-y follow-up, 4162 men, 14 873 women, aged 25+ y in 1963	Living with smoker or ex-smoker in 1963 (self-report); exposure to ex-smokers given less weight	1.31 men (1.1-1.6) (492) 1.24 women (1.1-1.4) (1539)	Small dose response for women only, adjusted for education
Svendsen et al[14]	7-y average follow-up for 1245 men aged 35-37 y, 1973-1982 MRFIT study (high-risk men)	Married to smoker (reported by husband)	1.61 (0.96-2.71) (90)	Positive dose response ($P = .2$), adjusted for 3 CV risk factors and education
Garland et al[15]	10-y follow-up, 695 women aged 50-79 y in 1972-1974	Married to smoker or ex-smoker (self-report)	2.9† ($P<.1$) (19; only 2 in nonexposed persons)	Age-adjusted positive dose response, small sample makes results unstable
Hirayama[16]	16-y follow-up study, 91 540 women aged 40+ y	Married to smoker or ex-smoker	1.10 (low), 1.31 (high) (No CI) (494)	Significant dose response, low to high exposure
Lee et al[17]	48 cases, 182 controls, 26 male cases, 22 female cases	*First marriage* to smoker or ex-smoker (self-report)	1.24 (men), 0.93 (women) (NS)	No dose response for total ETS exposure (not spouse alone), hospital-based
He[18]	34 female cases, 68 controls	Married to smoker for 5 or more y	3.00‡	Positive dose response, hospital-based, lacks details on methods
Dobson et al[19]	160 female cases, 183 male cases, 715 controls	Self-reported home exposure (time period not defined)	0.97 (men), 2.46 (women)‡	Ex-smokers had elevated risk (1.78 men, 1.48 women), no excess risk for workplace exposure, population-based

*ETS indicates environmental tobacco smoke; CI, confidence interval; IHD, ischemic heart disease; CV, cardiovascular; MRFIT, Multiple Risk Factor Intervention Trial; and NS, not significant. IHD mortality (classified as *International Classification of Diseases* [ICD] codes 410 through 414) is the end point for all studies except Humble et al,[12] which used all CV deaths (ICD classifications 390 through 456), and Lee et al,[17] He,[18] Dobson et al,[19] and Svendsen et al,[14] which used incidence.

†Estimated from data in article.

‡Significant at an undetermined level.

health effects based on known health effects of mainstream smoke (cigarette "equivalency") are not appropriate.

HEART DISEASE AND ETS

Epidemiologic evidence has been increasing that passive smoking at home is related to heart disease among never-smokers. Earlier reviews[1,9] concluded that the hypothesis associating ETS and heart disease was biologically plausible but that epidemiologic and experimental data were inconclusive.

A review of the recent literature shows that six new epidemiologic studies[10-15] have been published regarding ETS and heart disease. Table 1 summarizes all nine epidemiologic studies.[10-18] Seven are positive, while one is positive for women but not men. The five best-designed and largest studies[10-12,14,15] are cohort studies; three of the five controlled for the principal cardiovascular risk factors (cholesterol, blood pressure, and obesity), and three showed a positive dose response, while the other two showed a positive dose response for certain subgroups. A recent review of most of these studies[19] concluded that "heart disease is an important consequence of exposure to ETS" and estimated that the excess risk of heart disease for nonsmokers living with smokers was 30%.

The principal weaknesses in the epidemiologic evidence to date have been the indirect methods of assessing exposure (via spousal smoking) and the lack of data on exposures to ETS outside the home. If the effect of ETS on the coronary system is long-term, early exposures during childhood might also be important, but childhood exposures have not been considered in the epidemiologic studies. Also, there are many risk factors for heart disease, and it is difficult to control well for all of them.

Another problem with the epidemiologic data is the seemingly large effect that ETS has on heart disease compared with the effect of mainstream smoking. Active smoking is associated with heart disease, with a relative risk of smokers vs nonsmokers of about 1.7.[20] Most studies of never-smokers living with smokers indicate relative risks on the order of 1.2 to 1.3, compared with those of never-smokers living with never-smokers. These relative risks seem high compared with the risk for mainstream smoking. There are several counterarguments to this objection. Studies of mainstream smokers have used referent groups of never-smokers composed of never-smokers exposed to ETS and never-smokers not exposed to ETS, so that relative risks from mainstream and passive smoking studies are not directly comparable. Another argument is that dosimetry based on cigarette equivalents is misleading, since sidestream smoke is qualitatively different than mainstream smoke, and exposure to sidestream smoke may be proportionately more toxic to the heart than exposure to mainstream smoke.

Due to the relatively slight increased risk of heart disease for passive smokers and the many factors known to affect heart disease, the possibility of uncontrolled confounding as a cause for the increased risk cannot be ruled out. Confounding by dietary factors might bias disease risks for passive smokers upward. This suggestion is based on findings that never-smokers living with smokers have less nutritious diets than never-smokers living with nonsmokers.[21,22] The argument has principally been made for lung cancer risk and has focused on food containing carotenoids or retinoids, which are protective against lung cancer. A similar argument might be made for heart disease. However, several of the heart disease studies have adjusted for cholesterol, the most established heart disease risk factor related to diet. Furthermore, in one study,[21] never-smokers living with smokers ate significantly less cholesterol-containing food than never-smokers living with nonsmokers (while also eating significantly less carotenoid-containing vegetables). While carotenoids and retinoids may be protective against heart disease as they are against lung cancer, little published data support this claim.

An increasingly substantial body of animal and human experimental evidence supports the hypothesis that ETS increases the risk of heart disease. The 1986 National Research Council report noted that levels of carboxyhemoglobin (COHb) among those highly exposed to ETS was reported to be close to 3% and also noted

that animal and theoretical models suggested such levels might have adverse effects on the heart. However, the National Research Council found little evidence that ETS exposure in healthy subjects was detrimental. Since 1986 a series of new experimental studies have been reviewed by Glantz and Parmley,[19] who cite human evidence that ETS exposure (1) increases COHb and adversely affects exercise performance in both heart patients and healthy individuals; (2) increases platelet aggregation (at levels slightly less than those seen in active smokers) and adversely affects platelet function; and (3) damages the arterial endothelium (again at levels slightly less than those seen in active smokers). They also cite animal evidence that components of ETS (eg, polycyclic aromatic hydrocarbons) can increase the risk of atherosclerotic plaques. Hence, ETS might be thought to have either short-term effects on the heart (via COHb or thrombosis) or long-term effects (via endothelial damage and plaque development).

Two new human experimental studies lend further support to the adverse effect of ETS on the heart. Allred et al[23] studied 63 nonsmoking men with heart disease tested on a treadmill, after exposure to room air or to air with carbon monoxide levels of 117 ppm or 253 ppm (resulting in COHb levels of 0.6%, 2.0%, and 3.9%, respectively). The time to angina onset decreased significantly by 4.2% and 7.1% in those exposed to low and high carbon monoxide levels, respectively, compared with those exposed to room air. Sheps et al[24] studied 41 nonsmokers with coronary artery disease to assess the effects of carbon monoxide on ventricular arrhythmias. Patients performed a baseline bicycle exercise test and were exposed to room air (1.5% COHb), 100 ppm carbon monoxide (4% COHb), and 200 ppm carbon monoxide (6% COHb) over 3 days, followed by more exercise. Those with 6% COHb had significantly more arrhythmias during exercise than those exposed to only room air. When arrhythmias were weighted by severity, a dose response was observed.

The above experimental findings among heart patients exposed to carbon monoxide find epidemiologic support from a study of men exposed to high levels of carbon monoxide while working in New York City tunnels.[25] These men, exposed to carbon monoxide levels of approximately 50 ppm, suffered a 35% excess of IHD mortality compared with the US population, an excess that declined sharply after employment cessation (indicating a short-term effect). They showed no excess of lung cancer, and cross-sectional smoking data revealed smoking habits similar to the US referent population. Hence, increased cigarette smoking was unlikely to explain the excess heart disease risk.

Finally, recent evidence from two studies shows that exposure to ETS may lower levels of high-density lipoprotein cholesterol (HDL-C) and increase fibrinogen. Active smoking lowers HDL-C.[26] A recent study of never-smoking adults showed that those with ETS exposure (measured by urinary cotinine) had significantly lower HDL-C levels than adolescents without ETS exposure (7% lower) and significantly higher ratios of total cholesterol to HDL-C.[27] Another cross-sectional study[15] found higher levels of fibrinogen in nonsmokers exposed to ETS vs nonexposed nonsmokers. The authors suggested that higher fibrinogen levels might lead to increased thrombogenesis. While these studies were not longitudinal and provided evidence of a correlation but not causation, the data suggest other mechanisms by which ETS may contribute to cardiovascular disease.

In summary, recently published experimental and epidemiologic studies strengthen the case for a true association of ETS exposure and heart disease.

RISK ASSESSMENT

Risk assessment often means the development of a mathematical model to predict risks of disease based on a given quantified dose or exposure. Frequently, animal data are used, with doses well quantified. Assumptions are then required regarding the application of animal data to humans. Occasionally, epidemiologic (human) data are available with sufficient quantitative detail on exposure to permit such a risk assessment, but more often the data on exposure are qualitative (eg, exposed vs nonexposed), so that no quantitative dose response can be estimated. This is the case for ETS. However, two other types of risk assessment remain possible for ETS.[28]

The type used in this article is based on the epidemiologic literature and on the observed relative risk for never-smokers exposed to ETS vs those nonexposed. This type of risk assessment can be used to estimate the annual number of deaths due to ETS exposure among never-smokers in the United States. The excess lifetime risk for an individual never-smoker due to exposure to ETS (at an unknown average dose) beyond the background risk of a never-smoker with no ETS exposure can also be calculated. The most important assumption in this type of risk assessment is that there indeed is a real increase of risk for never-smokers exposed to ETS compared with those not exposed and that this increase in risk can be estimated from the existing epidemiologic studies. The estimates of population and individual risks are crude, but they provide a sense of the public health burden of heart disease due to ETS exposure.

Another method of risk assessment relies on models predicting the risk of mainstream smokers for heart disease by number of cigarettes smoked, and then estimates the equivalent number of cigarettes absorbed by nonsmokers exposed to ETS. However, this "dosimetric" method depends on too many assumptions about what is a "cigarette-equivalent dose" for those exposed to ETS, and so is not used here.

Presented herein are estimates of the number of IHD deaths due to ETS exposure among never-smokers, among former smokers who have quit 15 or more years previously, and among former smokers who quit 5 or more years previously. After quitting, smokers have a sharp reduction in heart disease risk (an estimated 50% in the first year), followed by a long decline in risk (a reduction in the long-term and presumably atherogenic effect), until reaching approximately the same risk as never-smokers after 15 years.[26] Hence, long-term former smokers (those who have not smoked for 15 or more years) can reasonably be considered as never-smokers. Former smokers with fewer years since quitting will have an increased risk from both ETS and their previous mainstream smoking, but the epidemiologic data to date do not permit a separation of these effects. Herein are calculated the ETS-attributable heart disease deaths for former smokers who quit 5 or more years previously, and it is assumed that the true number of ETS-attributable heart disease deaths for all former smokers lies somewhere between the attributable deaths for long-term former smokers (15 or more years) and short-term former smokers (5 or more years).

Current smokers are not considered here. Any additional IHD risk due to ETS exposure for current smokers is likely to be small compared with the effect of their mainstream smoking.

US DEATHS ATTRIBUTABLE TO IHD ANNUALLY

Formulas for Attributable Deaths

As shown in formula 1 below, the deaths attributable to IHD among never-smokers is

$$(EF_i)(d_i) = (EF_i)(I_i)(N_i),$$

where EF_i is the age-specific etiologic fraction, d_i is the age-specific number of IHD deaths among US never-smokers, I_i is the age-specific mortality rate from IHD among US never-smokers, and N_i are the age-specific person-years at risk

for US never-smokers.

The etiologic fraction is an epidemiologic measure to estimate the proportion of disease due to a specific exposure, based on the proportion of the population exposed and the relative risk due to the exposure.[29] In the context of passive smoking, it is defined[30] in formula 2 below as

$$EF = \frac{p(RR_1 - 1) + (1 - p)(RR_2 - 1)}{p(RR_1 - 1) + (1 - p)(RR_2 - 1) + 1}.$$

Here, p is the fraction of never-smokers exposed to ETS at home (living with a smoker), RR_1 is the rate ratio for never-smokers exposed to ETS at home vs never-smokers not exposed to ETS (the truly nonexposed), RR_2 is the rate ratio for never-smokers exposed to ETS at work or in social settings but not living with a smoker vs never-smokers not exposed to ETS (the truly nonexposed).

Derivation of RR_1 and RR_2

The RRs for IHD for never-smokers (1.31 for men and 1.24 for women) living with current or former smokers are from the study by Helsing et al,[10] the choice of which is dictated by several reasons. The goal here is to estimate the impact of ETS in the United States (other countries often have different types of tobacco and consumption patterns). The Helsing study is the only US study of IHD deaths in a large general population of both men and women. The study results are similar to the approximate results for all ETS-heart disease studies combined.[19] Choosing a point estimate of effect from a meta-analysis of all studies would yield about the same result. The Helsing study considered as exposed those never-smokers living with current smokers or ex-smokers, and hence assumes that heart disease can result from current exposure (a short-term effect) or past exposure (a long-term effect) from ETS. This definition of exposure is the one used in most studies of ETS and heart disease.

Two adjustments were made to these RRs prior to their use in formula 2 above, following the methods outlined by Wald et al.[31] The first adjustment is for the possibility that some people (approximately 7%) have been misclassified as never-smokers, but are current or former smokers. Such misclassification is potentially a serious problem. However, for heart disease this adjustment has little effect, largely because the heart disease RR for smokers compared with that for nonsmokers is relatively low (about 1.7). As a result of the adjustment, the RR for never-smoking men exposed to ETS decreased from 1.31 to 1.29, while the RR of 1.24 for women decreased to 1.22.

Table 2.—Attributable Deaths for Never-Smokers*

Sex and Age Group, y	US Population Never-Smokers, 1978-1980	IHD Rate per 100 000 Never-Smokers	Etiologic Fraction (Formula 2)	IHD Deaths Due to ETS† (Formula 1)
Women				
30-44	20 050 994	1.8	.2048	74
45-64	11 403 101	32.8	.2048	766
65+	9 748 043	921.3	.2048	18 390
Men				
30-44	13 748 852	2.8	.1900	73
45-64	4 564 316	161.7	.1900	1402
65+	3 086 316	1248.4	.1900	7321
Total				28 026

*IHD indicates ischemic heart disease; and ETS, environmental tobacco smoke. The last contains details of the formulas noted.
†These numbers are the products of the data in the second, third, and fourth columns.

The second adjustment has a greater effect and adjusts for background ETS exposure outside the home. The referent group of never-smokers living with nonsmokers was not truly nonexposed to ETS. It can be assumed that the referent group had an unknown increased rate of disease (b) compared with those truly nonexposed to any ETS. Never-smokers living with smokers showed about three times the cotinine as those living with nonsmokers.[7] If the increased rate of disease for never-smokers living with smokers should be about three times ($3b$) that of never-smokers living with nonsmokers but exposed to ETS outside the home (b), then according to formula 3,

$$\text{Observed RR} = 1 + 3b/1 + b.$$

Solving for b and using an observed RR of 1.29 for men, for male never-smokers living with smoking spouses, the RR for IHD death compared with that for never-smokers with no exposure to ETS (no exposure at home, work, or social settings) is 1.51, while the RR for male never-smokers not living with smoking spouses but exposed to background ETS at work or in social settings is 1.17 ($b = .17$). The corresponding RRs for women are 1.37 and 1.12. These adjusted RRs are used in the calculation of the etiologic fraction (formula 2 above).

The Fraction of Never-Smokers Living With Smokers

To calculate this fraction (the p in formula 2), data are taken from the never-smoking controls in four US case-control studies of lung cancer and ETS, conducted in the late 1970s and early 1980s.[32-35] These studies involved 658 men and 878 women, of whom 19% and 55% had spouses who were smokers or ex-smokers. Age-specific exposure prevalence was not available from these studies. Age-specific data from 778 female controls in a recent US lung cancer case-control study (Elizabeth Fontham, PhD, written communication, July 1991) tend to confirm the overall estimate for women and show little difference in the percentage exposed after the age of 45 years.

Approximately 75% of US adults are married.[36] The assumption made here is that the married and unmarried individuals are alike regarding their potential for exposure to ETS. Some data justify this assumption, based on urinary cotinine levels of single women.[2]

IHD Rates Attributable to ETS

Age-specific (at 5-year intervals) and sex-specific IHD rates for US never-smokers were estimated using data from four cohort studies: (1) the cohort study conducted by the American Cancer Society[36] (follow-up 1982 through 1985) (Lawrence Garfinkel, MA, American Cancer Society, written communication, June 1990); (2) the US veterans cohort study[37] (follow-up 1975 through 1980, men only) (Aaron Blair, PhD, National Cancer Institute, written communication, June 1991); (3) the Seventh-Day Adventist cohort study[38] (follow-up 1977 through 1982) (Paul Mills, PhD, Loma Linda University, written communication, June 1991), and the Nurses Health Study[39] (follow-up 1976 through 1988, women only) (Graham Colditz, MD, Nurses Health Study, written communication, July 1991). To combine these rates, unweighted averages (three studies per sex) were taken of the age- and sex-specific rates, and direct standardization (with the 1980 US population as the standard) was used to create summary rates for the three age categories in this review (<45, 45-64, 65+ years).

Estimates of the age- and sex-specific number of never-smokers in the United States were obtained from the 1978 through 1980 National Health Interview Surveys[40] (and Robert Brackbill, PhD, National Institute for Occupational Safety and Health, written communication, April 1991).

Table 3 — Attributable Deaths for Former Smokers*

Sex and Age Group, y	US Population of Former Smokers (%)	IHD Rate per 100 000 Never-Smokers	Etiologic Fraction (Formula 2)	IHD Deaths Due to ETS† (Formula 1)
Smokers Quitting 15 or More Years Previously				
Women				
30-44	423 596 (7)	1.8	.2048	2
45-64	1 126 576 (28)	32.8	.2048	76
65+	709 214 (36)	921.3	.2048	1338
Men				
30-44	781 003 (10)	2.8	.1900	4
45-64	1 924 411 (28)	161.7	.1900	591
65+	2 114 671 (36)	1248.4	.1900	5016
Total				7027
Smokers Quitting 5 or More Years Previously				
Women				
30-44	2 440 161 (41)	1.8	.2048	9
45-64	2 602 232 (66)	32.8	.2048	175
65+	1 338 545 (69)	921.3	.2048	2525
Men				
30-44	3 671 518 (46)	2.8	.1900	19
45-64	4 709 387 (70)	161.7	.1900	1447
65+	3 512 504 (78)	1248.4	.1900	8332
Total				12 507

*IHD indicates ischemic heart disease; and ETS, environmental tobacco smoke. The text contains details of the formulas noted.

†These numbers are the product of the data in the second, third, and fourth columns.

Multiplying these rates and population estimates by the etiologic fraction, approximately 28 027 deaths among US never-smokers are estimated to have occurred annually in the 1980s as a result of ETS exposure (Table 2).

Similar data for former smokers who quit 15 or more years previously are summarized in Table 3, based on the assumption that they have approximately the same relative risk and proportions exposed as never-smokers. Also presented are attributable deaths under the assumption that former smokers who quit 5 or more years previously have the same risks from passive smoking as do never-smokers. These last data indicate how attributable deaths increase under a variety of assumptions about the return of former smokers to baseline (never-smoker) risk. The final estimates of attributable deaths are presented as a range, assuming that the true number of ETS-attributable IHD deaths among former smokers lies between the number derived in considering only former smokers who quit more than 15 years previously and the number derived by considering former smokers with 5 or more years since quitting (Table 3). Combining the above estimates, the overall estimate of ETS-attributable heart disease deaths for never-smokers and former smokers is 35 000 to 40 000.

IHD RISK FOR NEVER-SMOKERS LIVING WITH SMOKERS

Individual excess risk of death for a never-smoker exposed to ETS can be derived using an RR estimate and converting rates for never-smokers to a cumulative risk of IHD death by a given age, using formula 4 below, which accounts for competing causes of death[41]:

$$\text{Excess risk} = \sum_{i=30}^{74} (RR_i - 1) q_i(i) \exp\left[-\sum_{j=30}^{i} (RR_j - 1) q_i(j) + q_a(j)\right]$$

In formula 4 excess risk refers to cumulative excess risk of IHD death by the age of 74 years, q_i is the IHD mortality rate for nonexposed (truly nonexposed, no ETS exposure in home or elsewhere), q_a is the overall all-causes mortality rate for the nonexposed (here assumed to be the all-causes mortality rate for never-smokers) (age- and sex-specific data for 1982 through 1984 provided by Lawrence Garfinkel, MA, American Cancer Society, written communication, June 1990), RR is the rate ratio for the exposed vs the nonexposed (assumed to be constant over age), and i and j index ages. Background risk for never-smokers may be calculated by omitting the terms using the RRs. An Axelson-type adjustment[42] was used to derive the background IHD rate for the truly nonexposed. The Axelson technique consists of partitioning the overall IHD mortality rate for never-smokers into a weighted average of the rate for those with background exposure (the rate for the truly nonexposed times the RR for never-smokers with background ETS exposure) and the rate for those living with smokers (the rate for the truly nonexposed times the RR for never-smokers living with smokers). The resulting equation may then be solved for the rate of those truly nonexposed.

For a female never-smoker with no ETS exposure (truly nonexposed), the lifetime (to an average age of 79 years) risk of IHD death is 4.4%. The risk for a female never-smoker exposed to background ETS exposure is 4.9%, while the risk for a female never-smoker living with a smoker is 6.1%. Corresponding results for men from age 30 to an average age of 74 years are 6.3%, 7.4%, and 9.6%. These results should be viewed as crude estimates, given the multiple assumptions involved. These risks apply to long-term former smokers.

The estimated increased risks of death from IHD due to ETS exposure are higher than those accepted in regulating environmental toxins. For example, environmental limits for toxins are often set to limit the number of excess deaths resulting from exposure to one in 10^5 or one in 10^6,[43] whereas the excess risks calculated are in the range of one to three per 100. There are currently no federal regulations regarding exposure to ETS, with the exception of regulation for domestic airline flights.

CONCLUSION

A number of assumptions are involved in estimating the heart disease mortality due to ETS, adding an unfortunate level of uncertainty. The most important assumption is that the relative risks for ETS and heart disease, derived from the epidemiologic evidence, are reasonably accurate. The epidemiologic results may be questioned, given the inherent uncertainties of any epidemiologic study. Differential misclassification of ever-smokers as never-smokers and uncontrolled confounding are possible explanations for the excess risk observed in the epidemiologic studies. However, neither of these likely accounts for the observed risks. The epidemiologic data are strengthened because multiple studies now are consistent and reasonably well designed.

Considerable uncertainty is involved in extrapolating from the epidemiologic data, which consider the relative risks for never-smokers living with smokers, to estimating relative risks for those exposed to ETS (anywhere) vs those truly not exposed (anywhere). This latter population of the truly nonexposed is largely hypothetical, in that virtually everyone is exposed to background levels. This extrapolation was made based on observed relative risks for ETS exposure at home and on urinary cotinine measurements, but is necessarily a crude estimate. If it were assumed that background (not from spouse) exposure causes no increase in risk (ie, a threshold effect), then the number of annual IHD-attributable deaths (due solely to

exposure from a spouse) drops to about 15 000 to 19 000.

The above estimate of 35 000 to 40 000 IHD deaths attributable to ETS among never-smokers and former smokers is based on data from the early 1980s. The current number of attributable deaths is likely to be lower, given the declining prevalence of smoking, declining heart disease mortality, and the increased societal trend to limit exposure to ETS.

One prior risk assessment of ETS and heart disease exists, using methods similar to those used here. Wells[44] estimated that in the United States in 1985 there were 32 000 heart disease deaths among nonsmokers (never-smokers and former smokers) attributable to ETS. His estimate is surprisingly close to the one presented herein, despite the fact that he used different data and assumptions in his estimate. Wells included all former smokers in the population at risk for ETS-induced heart disease, while my discussion is restricted to never-smokers and former smokers with at least 5 years since quitting. Wells extrapolated American Cancer Society data from the 1960s for heart disease rates among never-smokers to estimate these rates for the 1980s. I have used never-smoker heart disease rates from four cohort studies in the 1970s and 1980s. Wells used a different procedure to estimate the prevalence and effect of exposure outside the home.

In this article the assumption has been made that never-smokers living with current or former smokers have an increased risk of heart disease. That is, both short-term and long-term effects of ETS on the heart have been assumed. This assumption agrees with the epidemiologic evidence, which in most studies has defined exposure as living with a current smoker or an ex-smoker. If one were to assume the effect of ETS on the heart were only short-term (eg, via an increase in COHb), then one would have to use RRs from studies in which exposure is defined as living with a current smoker. There are two US studies using this definition of exposure.[12,16] Both show a higher RR for exposed vs nonexposed (approximately 1.6) than the one assumed here (1.2 to 1.3). However, these studies have limitations for use in calculating attributable risk. One[12] included only women and the outcome was based on all circulatory disease (including stroke), not IHD. The other[16] included only men at high risk of heart disease.

In conclusion, assuming the epidemiologic evidence is valid and assuming our estimate of 35 000 to 40 000 annual excess heart disease deaths among never-smokers and long-term former smokers due to passive smoking is correct, then heart disease mortality is contributing the bulk of the public health burden imposed by passive smoking. Lung cancer, the previous main culprit, has been estimated to cause approximately 3000 excess deaths per year among never-smokers.

Comments on earlier versions of the manuscript were kindly provided by Drs Judson Wells, Peter Gann, Leslie Stayner, Lewis Kuller, and Thomas Robins.

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